

Atty Dkt. No.: 10001492-2
USSN: 10/052,926

AMENDMENTS TO THE CLAIMS

Please incorporate the following amendments to the subject application.

In the Claims:

1. (Previously Presented) A method of sequencing a nucleic acid molecule comprising steps of:
providing two separate, adjacent pools of a medium and an interface between the two pools, the interface having a channel so dimensioned as to allow sequential nucleotide-by-nucleotide passage from one pool to the other pool of only one nucleic acid molecule at a time;
providing a nucleic acid molecule with at least one repeat of a nucleotide sequence to be determined, wherein the nucleic acid molecule is enzymatically synthesized using a circular template, and wherein the nucleic acid molecule contains modified nucleotides that reduce secondary structure in the nucleic acid molecule;
placing the nucleic acid molecule in one of the two pools; and
taking measurements as each of the nucleotides of the nucleic acid molecule passes through the channel so as to determine the sequence of the nucleic acid molecule.
2. (Original) The method of claim 1, wherein the nucleic acid is single-stranded.
3. (Original) The method of claim 2, wherein the nucleic acid is single-stranded DNA.
4. (Previously Presented) The method of claim 2, wherein the nucleic acid is single-stranded RNA.
5. (Original) The method of claim 1, wherein the nucleic acid is an unstructured nucleic acid.
6. (Original) The method of claim 1, wherein the circular template is single-stranded.
7. (Original) The method of claim 1, wherein the circular template is double-stranded.

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8. (Original) The method of claim 1, wherein the medium is electrically conductive.
9. (Original) The method of claim 8, wherein the medium is an aqueous solution.
10. (Original) The method of claim 9, further comprising applying a voltage across the interface.
11. (Original) The method of claim 10, wherein ionic flow between the two pools is measured.
12. (Original) The method of claim 11, wherein the duration of ionic flow blockage is measured.
13. (Original) The method of claim 11, wherein the amplitude of ionic flow blockage is measured.
14. (Original) The method of claim 8, further comprising applying a voltage across the interface.
15. (Original) The method of claim 14, wherein ionic flow between the two pools is measured.
16. (Original) The method of claim 15, wherein the duration of ionic flow blockage is measured.
17. (Original) The method of claim 15, wherein the amplitude of ionic flow blockage is measured.
18. (Original) The method of claim 1, wherein the nucleic acid polymer interacts with an inner surface of the channel.
19. (Original) The method of claim 18, wherein the medium is electrically conductive.
20. (Original) The method of claim 19, wherein the medium is an aqueous solution.
21. (Original) The method of claim 20, further comprising applying a voltage across the interface.
22. (Original) The method of claim 21, wherein ionic flow between the two pools is measured.
23. (Original) The method of claim 22, further comprising applying a voltage across the interface.

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24. (Original) The method of claim 23, wherein ionic flow between the two pools is measured.
25. (Original) The method of claim 24, wherein the duration of ionic flow blockage is measured.
26. (Original) The method of claim 25, wherein the amplitude of ionic flow blockage is measured.
27. (Original) The method of claim 1, further comprising providing a polymerase or exonuclease in one of the two pools, wherein the polymerase or exonuclease draws the nucleic acid polymer through the channel.
28. (Original) The method of claim 27, wherein the medium is an aqueous solution.
29. (Original) The method of claim 28, wherein ionic flow between the two pools is measured.
30. (Original) The method of claim 27, wherein ionic flow between the two pools is measured.
31. (Original) The method of claim 1, wherein the nucleic acid molecule contains modified adenosine and modified thymine which are not able to form base pairs, wherein the modified adenosine is capable of forming a base pair with unmodified thymine, and wherein the modified thymine is capable of forming a base pair with unmodified adenosine.
32. (Original) The method of claim 1, wherein the nucleic acid molecule contains modified guanosine and modified cytosine which are not able to form base pairs, wherein the modified guanosine is capable of forming a base pair with unmodified cytosine, and wherein the modified cytosine is capable of forming a base pair with unmodified guanosine.
33. (Original) The method of claim 1, wherein the nucleic acid molecule contains 2-aminoadenosine, 2-thiothymidine, inosine, and pyrrolopyrimidine.
34. (Original) The method of claim 1, wherein the nucleic acid molecule contains 2-aminoadenosine, and 2-thiothymidine.
35. (Original) The method of claim 1, further comprising analyzing the nucleic acid molecules by electron tunneling.
36. - 66. (Cancelled)

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67. (Previously Presented) A method of sequencing a nucleic acid molecule comprising steps of:

providing two separate, adjacent pools of a medium and an interface between the two pools, the interface having a channel so dimensioned as to allow sequential nucleotide-by-nucleotide passage from one pool to the other pool of only one nucleic acid molecule at a time;

providing a nucleic acid molecule with modified nucleotides that reduce secondary structure in the nucleic acid molecule;

placing the nucleic acid molecule in one of the two pools; and

taking measurements as each of the nucleotides of the nucleic acid molecule passes through the channel so as to determine the sequence of the nucleic acid molecule.

68. (Original) The method of claim 67, wherein the nucleic acid is single-stranded.

69. (Original) The method of claim 68, wherein the nucleic acid is single-stranded DNA.

70. (Original) The method of claim 68, wherein the nucleic acid is single-stranded RNA.

71. (Original) The method of claim 67, wherein the nucleic acid is an unstructured nucleic acid.

72. (Original) The method of claim 67, wherein the circular template is single-stranded.

73. (Original) The method of claim 67, wherein the circular template is double-stranded.

74. (Original) The method of claim 67, wherein the nucleic acid molecule contains modified adenosine and modified thymine which are not able to form base pairs, wherein the modified adenosine is capable of forming a base pair with unmodified thymine, and wherein the modified thymine is capable of forming a base pair with unmodified adenosine.

75. (Original) The method of claim 67, wherein the nucleic acid molecule contains modified guanosine and modified cytosine which are not able to form base pairs, wherein the modified guanosine is capable of forming a base pair with

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unmodified cytosine, and wherein the modified cytosine is capable of forming a base pair with unmodified guanosine.

76. (Original) The method of claim 67, wherein the nucleic acid molecule contains 2-aminoadenosine, 2-thiothymidine, inosine, and pyrrolopyrimidine.

77. (Original) The method of claim 67, wherein the nucleic acid molecule contains 2-aminoadenosine, and 2-thiothymidine.

78. (Original) The method of claim 67, wherein the medium is electrically conductive.

79. (Original) The method of claim 78, wherein the medium is an aqueous solution.

80. (Original) The method of claim 79, further comprising applying a voltage across the interface.

81. (Original) The method of claim 80, wherein ionic flow between the two pools is measured.

82. (Original) The method of claim 81, wherein the duration of ionic flow blockage is measured.

83. (Original) The method of claim 81, wherein the amplitude of ionic flow blockage is measured.

84. (Original) The method of claim 78, further comprising applying a voltage across the interface.

85. (Original) The method of claim 84, wherein ionic flow between the two pools is measured.

86. (Original) The method of claim 85, wherein the duration of ionic flow blockage is measured.

87. (Original) The method of claim 84, wherein the amplitude of ionic flow blockage is measured.

88. (Original) The method of claim 67, wherein the nucleic acid polymer interacts with an inner surface of the channel.

89. (Original) The method of claim 88, wherein the medium is electrically conductive.

90. (Original) The method of claim 89, wherein the medium is an aqueous solution.

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91. (Original) The method of claim 90, further comprising applying a voltage across the interface.
92. (Original) The method of claim 91, wherein ionic flow between the two pools is measured.
93. (Original) The method of claim 92, further comprising applying a voltage across the interface.
94. (Original) The method of claim 93, wherein ionic flow between the two pools is measured.
95. (Original) The method of claim 94, wherein the duration of ionic flow blockage is measured.
96. (Original) The method of claim 94, wherein the amplitude of ionic flow blockage is measured.
97. (Original) The method of claim 67, further comprising providing a polymerase or exonuclease in one of the two pools, wherein the polymerase or exonuclease draws the nucleic acid polymer through the channel.
98. (Original) The method of claim 97, wherein the medium is an aqueous solution.
99. (Original) The method of claim 98, wherein ionic flow between the two pools is measured.
100. (Original) The method of claim 97, wherein ionic flow between the two pools is measured.
101. (Original) The method of claim 67, further comprising analyzing the nucleic acid by electron tunneling.
102. - 143. (Cancelled)
144. (Previously Presented) The method of claim 1, wherein the nucleic acid molecule contains a modified thymine.
145. (Previously Presented) The method of claim 1, wherein the nucleic acid molecule contains 2-thiothymidine.
146. (Previously Presented) The method of claim 67, wherein the nucleic acid molecule contains a modified thymine.
147. (Previously Presented) The method of claim 67, wherein the nucleic acid molecule contains 2-thiothymidine.

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148. (New) The method of claim 1, which further comprises producing said provided nucleic acid.

149. (New) The method of claim 67, which further comprises producing said provided nucleic acid.